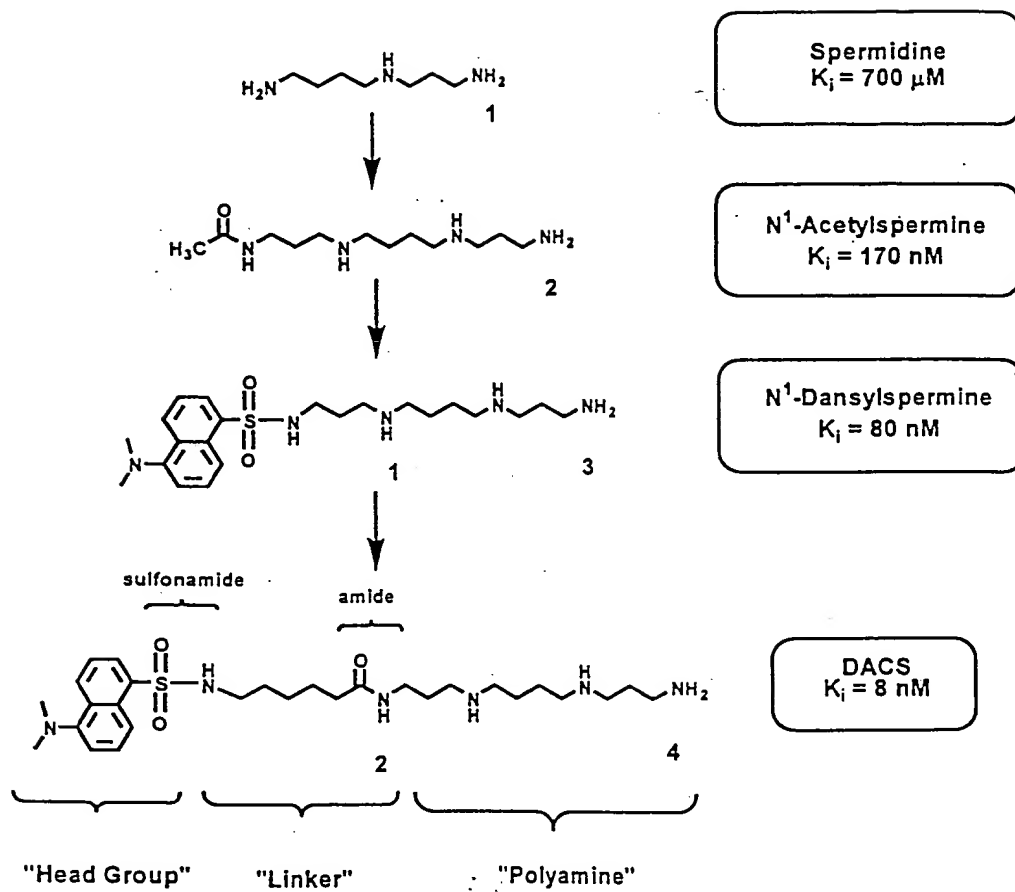


Fig. 1



00477-2554-11400

#	Structure	Ki (M) <sup>a</sup>	R <sup>b</sup>	Method <sup>c</sup>
3		0.080	20	I
4		0.010	400	IX, XIII
5		0.010	210	XIII
6		0.005	220	XIII
7		0.10	3.6	III
8		0.110	3.7	II
9		0.440	2.7	IV
10		0.050	>10	XV
11		0.190	2.4	XV

<sup>a</sup> Inhibition of polyamine uptake: Ki determined from Lineweaver-Burke double reciprocal plots  
<sup>b</sup> Inhibition of Tumor Cell Growth: R is ratio of IC50 (compound alone) to IC50 (compound + DFMO)  
<sup>c</sup> Numbers refer to Examples (describing synthesis)  
<sup>d</sup> Purchased from Aldrich Chemical Company

Fig. 2/1

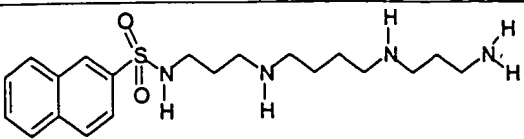
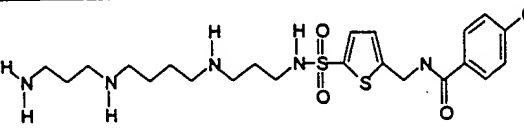
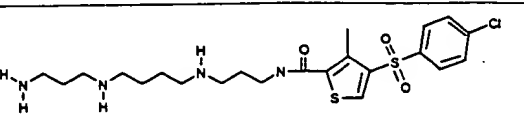
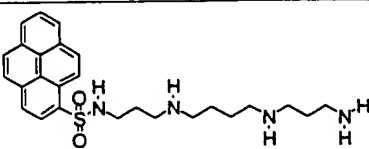
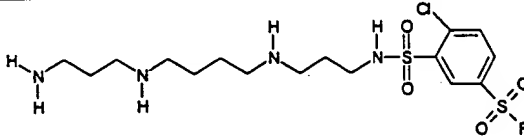
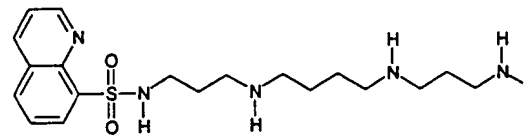
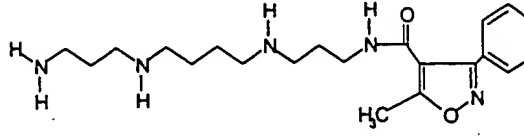
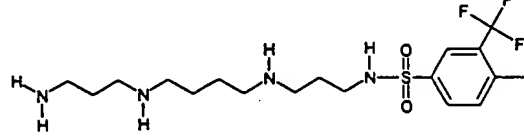
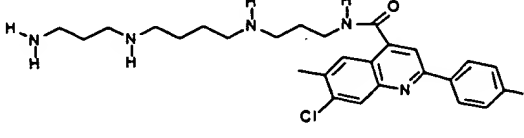
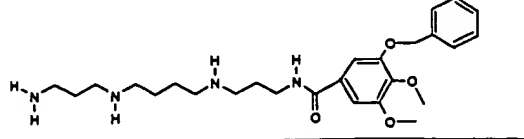
#	Structure	Ki (M) <sup>a</sup>	R <sup>b</sup>	Method <sup>c</sup>
12		0.150	4.3	XV
13		0.058	>47	XV
14		0.037	14	XVII
15		0.091	2.2	II
16		0.08	2.1	XV
17		0.43	>31	XV
18		0.083	40	XVII
19		0.24	>10	XV
20		0.28	1.0	XVII
21		0.084	1.0	XVII

Fig. 2/2

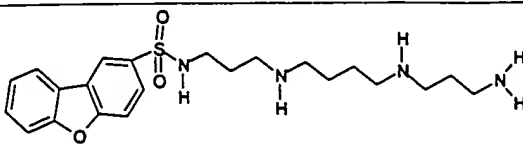
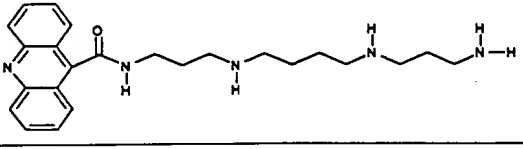
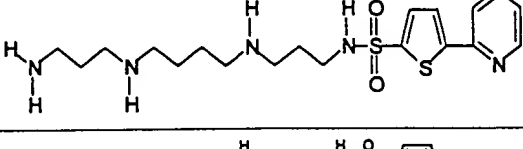
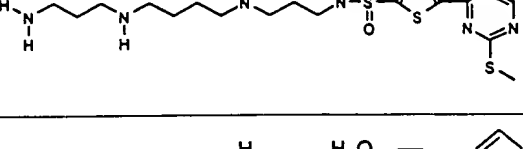
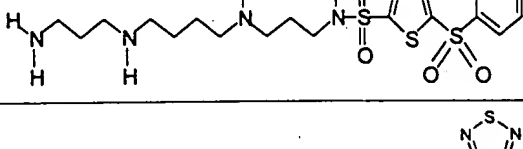
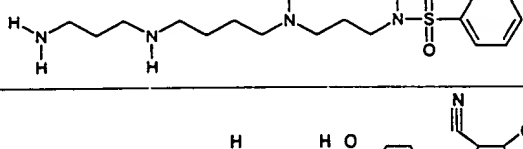
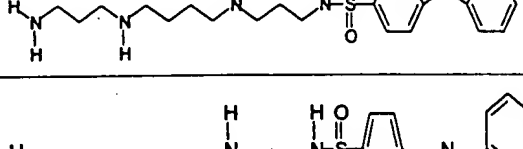
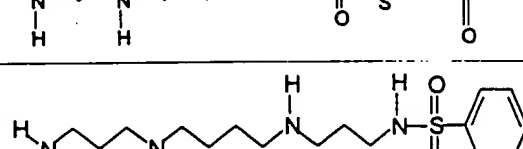
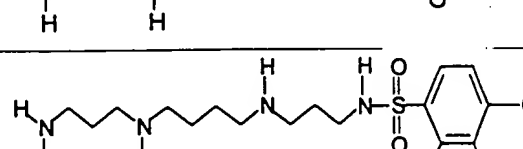
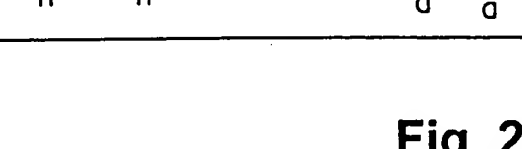
#	Structure	Ki (M) <sup>a</sup>	R <sup>b</sup>	Method <sup>c</sup>
22		0.066	11	XV
23		0.250	6.2	II
24		0.23	10	XV
25		0.067	8.6	XV
26		0.180	15	XV
27		0.650	9.9	XV
28		0.054	9.3	XV
29		0.076	>46	XV
30		0.120	>10	XV
31		0.083	>12	XII

Fig. 2/3

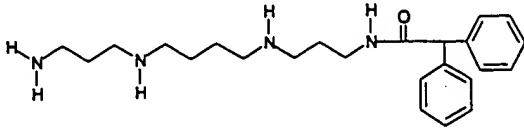
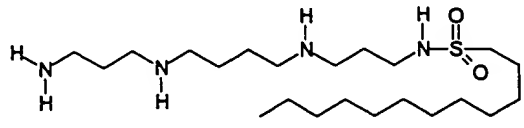
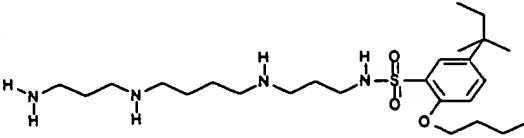
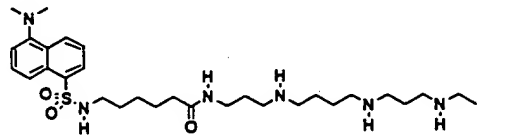
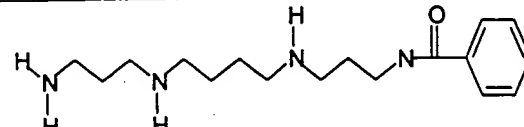
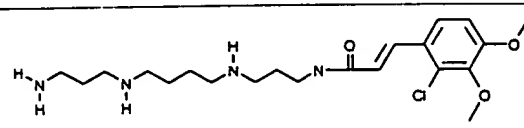
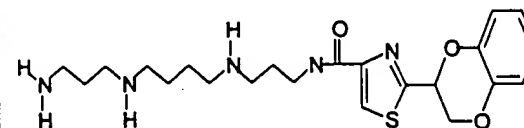
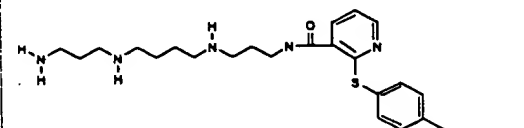
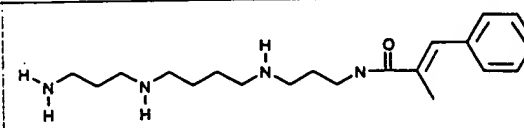
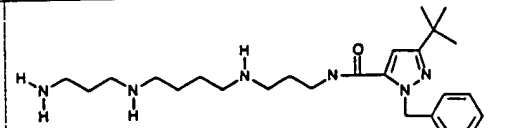
#	Structure	Ki (M) <sup>a</sup>	R <sup>b</sup>	Method <sup>c</sup>
32		0.093	2.1	XVII
33		0.17	1.4	XV
34		0.120	1.0	XV
35		0.041	33	XIII
36		0.61	>2	XVII
37		0.150	2.4	XVII
38		0.140	1.0	XVII
39		0.500	1	XVII
40		0.086	18	XVII
41		0.200	1.0	XVII

Fig. 2/4

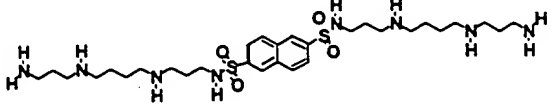
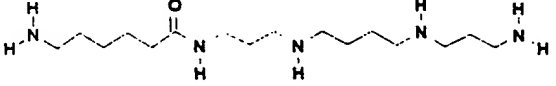
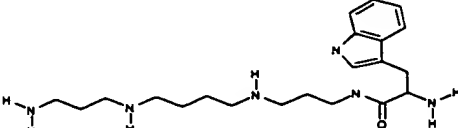
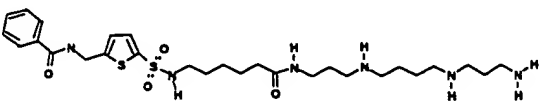
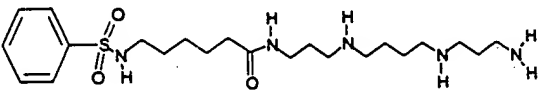
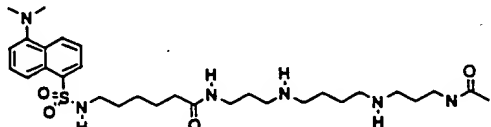
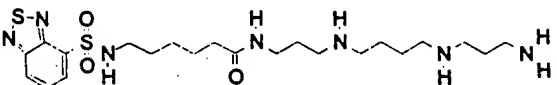
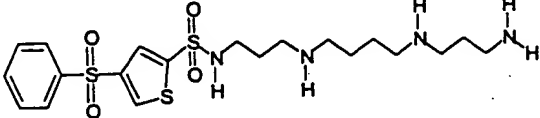
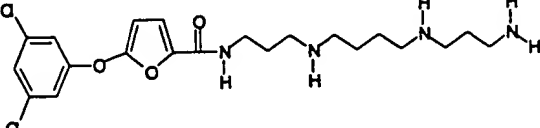
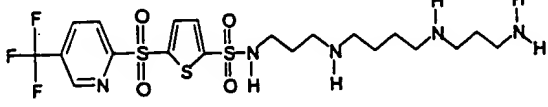
#	Structure	Ki (M) <sup>a</sup>	R <sup>b</sup>	Method <sup>c</sup>
42		0.110	1.1	XIV
43		0.033	76	XVII
44		0.073	39	XIII
45		0.052	3.0	XIII
46		0.082	63	XIII
47		2.1	6.8	XIII
48		0.079	>49	XIII
49		0.067	3.2	XV
50		0.12	1.0	XVII
51		0.083	1.5	XV

Fig. 2/5

#	Structure	Ki (M) <sup>a</sup>	R <sup>b</sup>	Method <sup>c</sup>
52		0.094	5.3	XV
53		0.18	1.0	XV
54		0.19	2.0	XV
55		0.079	>1.1	IV
56		0.190		d
57		0.017	170	XV
58		0.050	189	XIII
59			>1	XIII
60			>1	XIII
61		0.200	1.0	XIII

Fig. 2/6

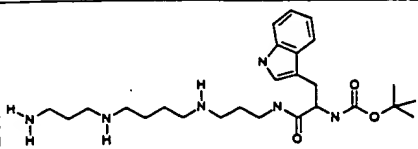
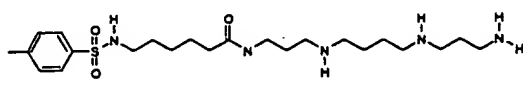
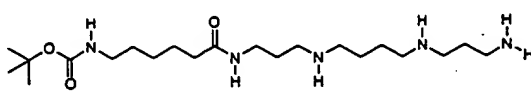
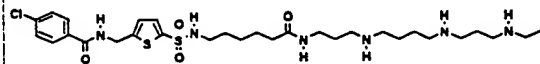
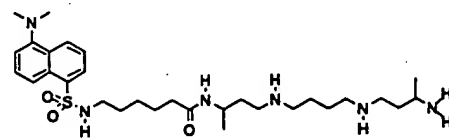
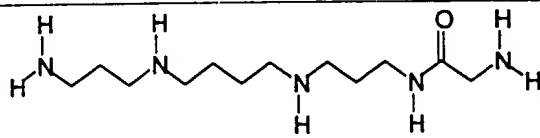
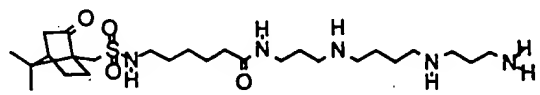
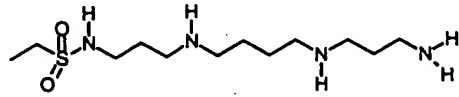
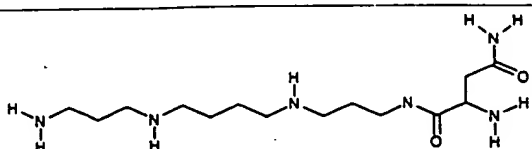
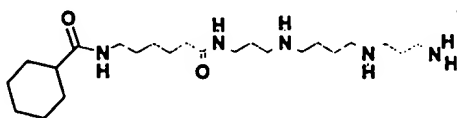
#	Structure	Ki (M) <sup>a</sup>	R <sup>b</sup>	Method <sup>c</sup>
62			>2.0	XIII
63		0.050	>1	XIII
64		0.046		XIII
65		0.012		XIII
66		0.018	27	XIII
67		0.07	1.0	XIII
68		0.110	>4.4	XIII
69		0.22	1	XV
70		0.033	>12.2	XIII
71		0.160	>1.5	XIII

Fig. 2/7



#	Structure	Ki (M) <sup>a</sup>	R <sup>b</sup>	Method <sup>c</sup>
72		0.031	>100	XIII
73		0.094	>1	XIII
74		0.200	1.0	XIII
75		0.130	>1	XIII
76		0.040	1.0	XIII
77		0.093	1	XIII
78		0.156		XIII
79		0.047	1	XIII
80		0.258		XIII
81		0.0096	153	XIII

Fig. 2/8

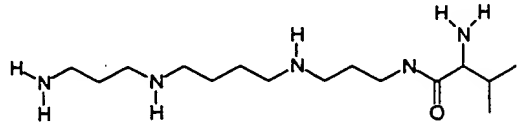
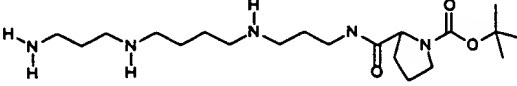
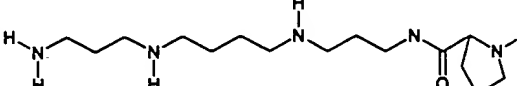
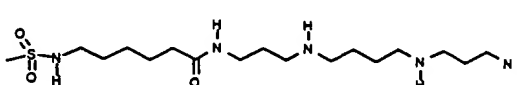
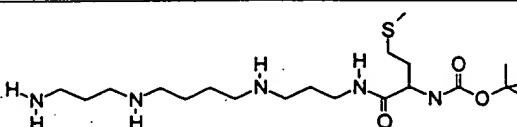
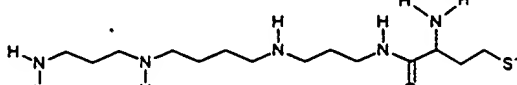
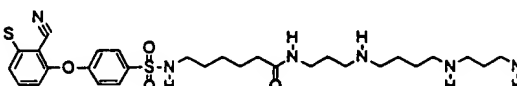
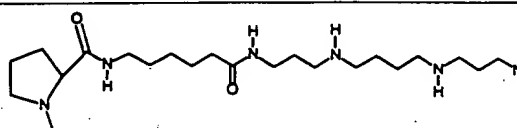
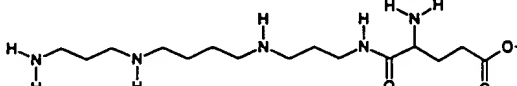
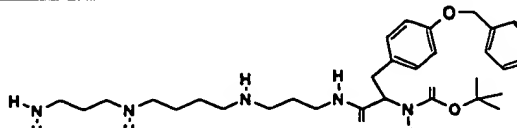
#	Structure	Ki (M) <sup>a</sup>	R <sup>b</sup>	Method <sup>c</sup>
82		0.097	>54	XIII
83		0.183		XIII
84		0.036	>3.2	XIII
85		0.048	>6.5	XIII
86		0.091		XIII
87		0.034	>1	XIII
88		0.014	>40	XIII
89		0.020	>1	XIII
90		0.077		XIII
91		0.037	1	XIII

Fig. 2/9

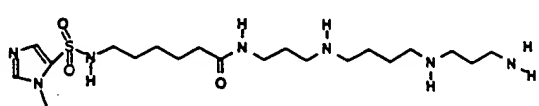
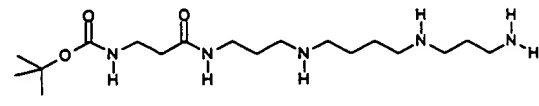
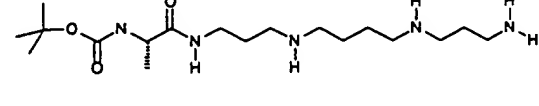
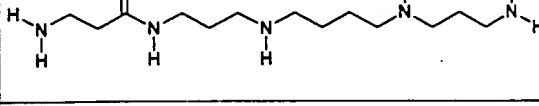
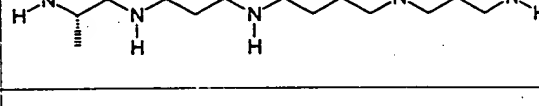
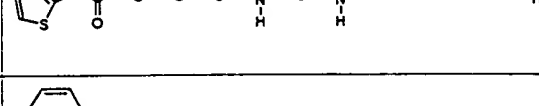
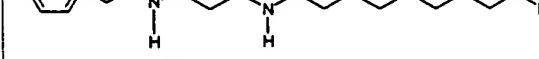
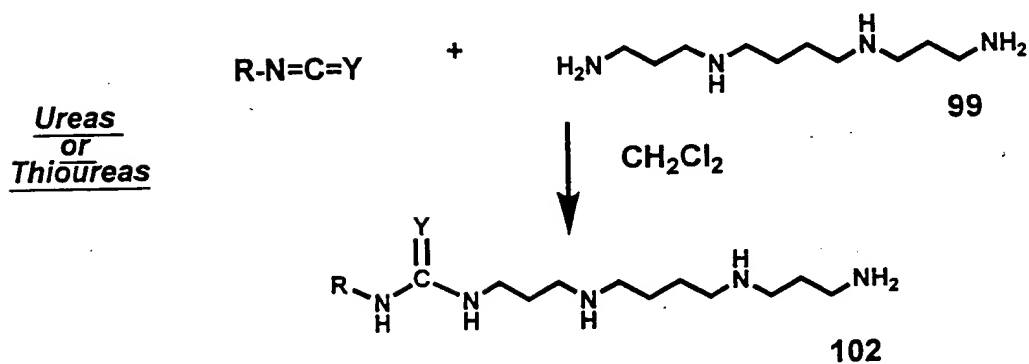
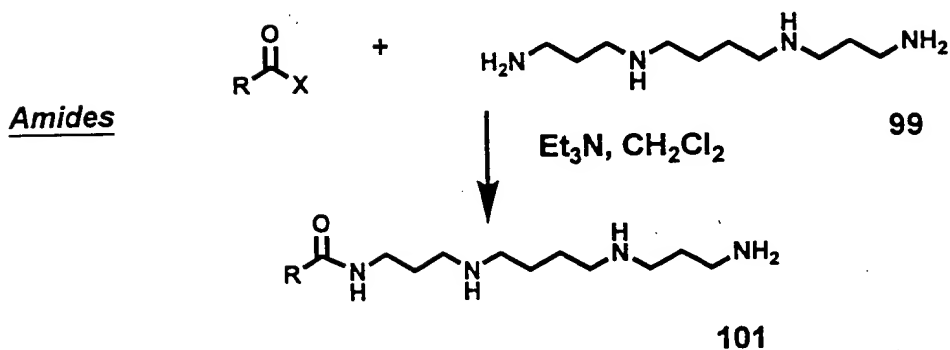
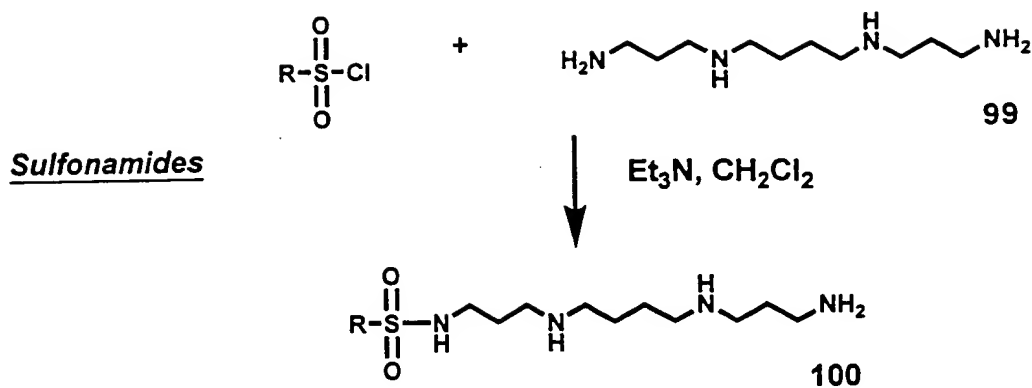
#	Structure	Ki (M) <sup>a</sup>	R <sup>b</sup>	Method <sup>c</sup>
92		0.300	1	XIII
93		0.061	1	XIII
94		0.042	1	XIII
95		0.050	1	XIII
96		0.034	1	XIII
97		0.027	1	XIII
98		0.180	12	d

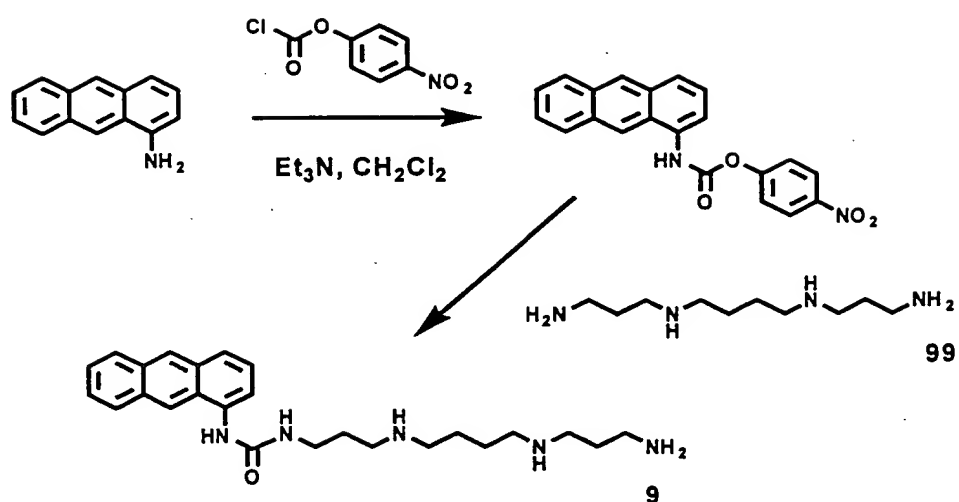
Fig. 2/10

Fig. 3



Where **X** = halide or N-hydroxysuccinimide ester  
**R** = head group  
polyamine = spermine (or other)  
**Y** = O or S or NHR  
(corresponding to ureas, thioureas and guanidines, respectively)

**Fig. 4**



**Fig. 5**

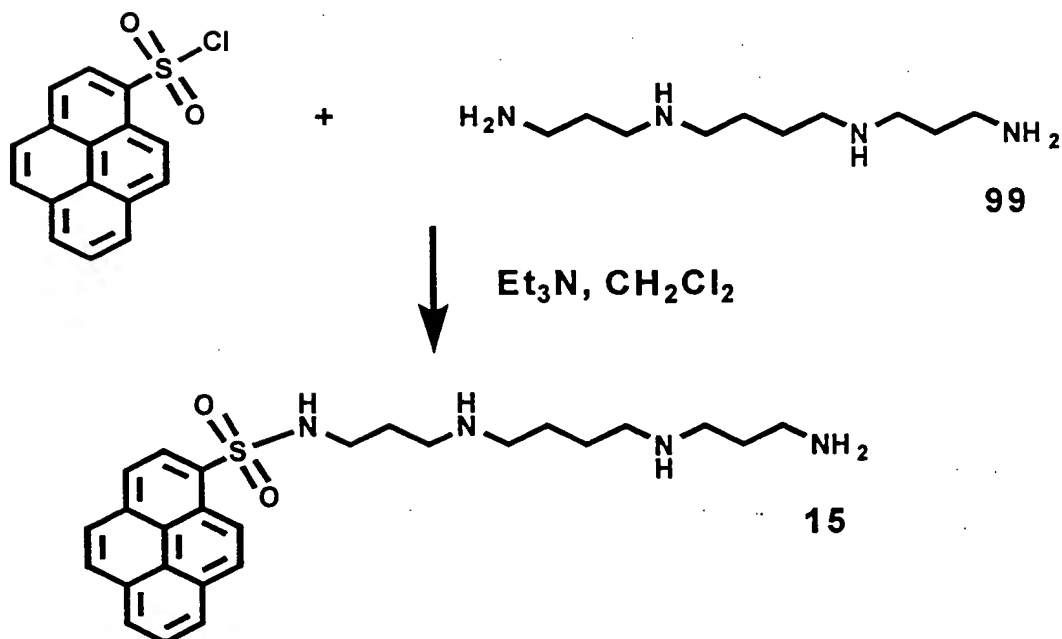


Fig. 6

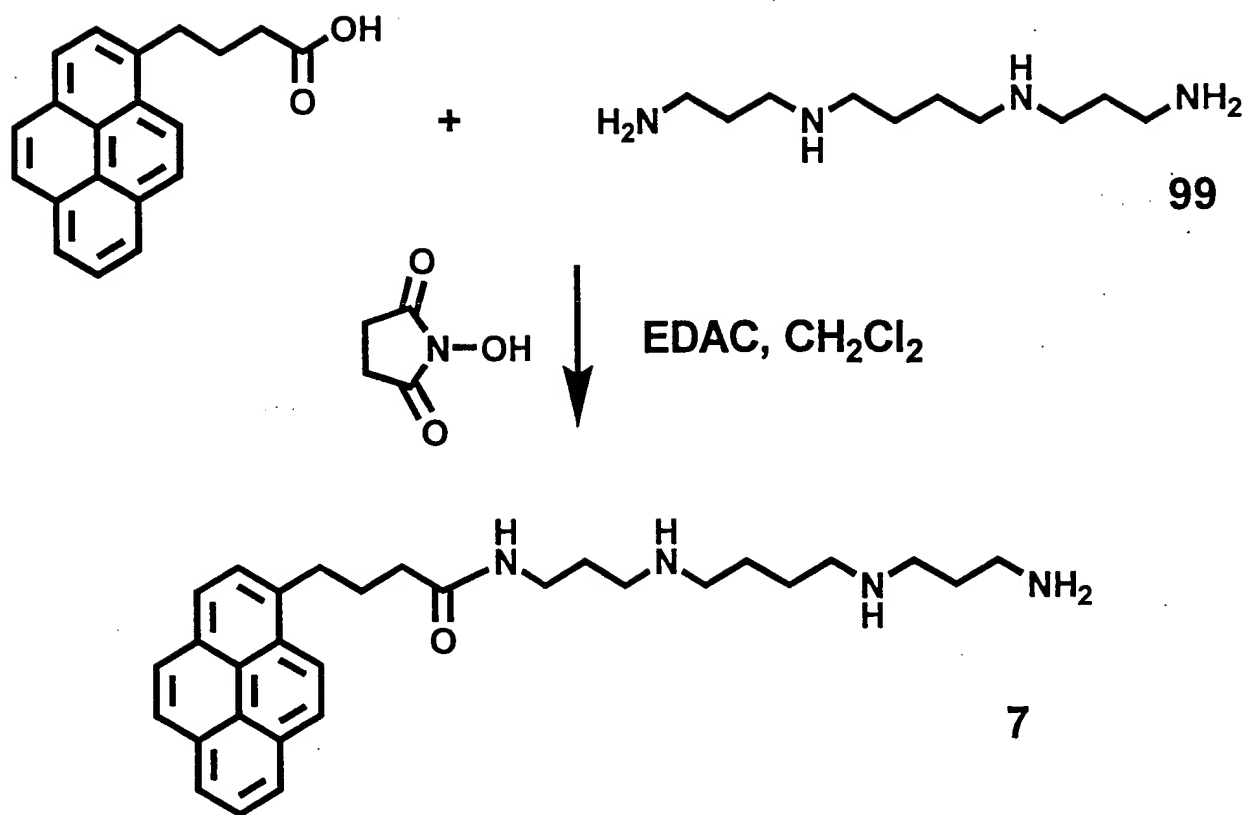


Fig. 7

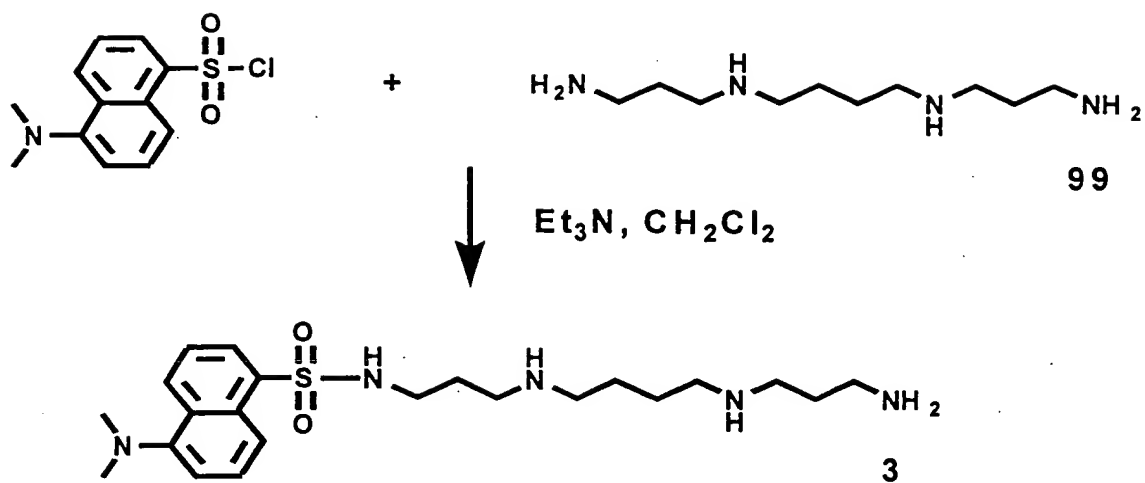


Fig. 8

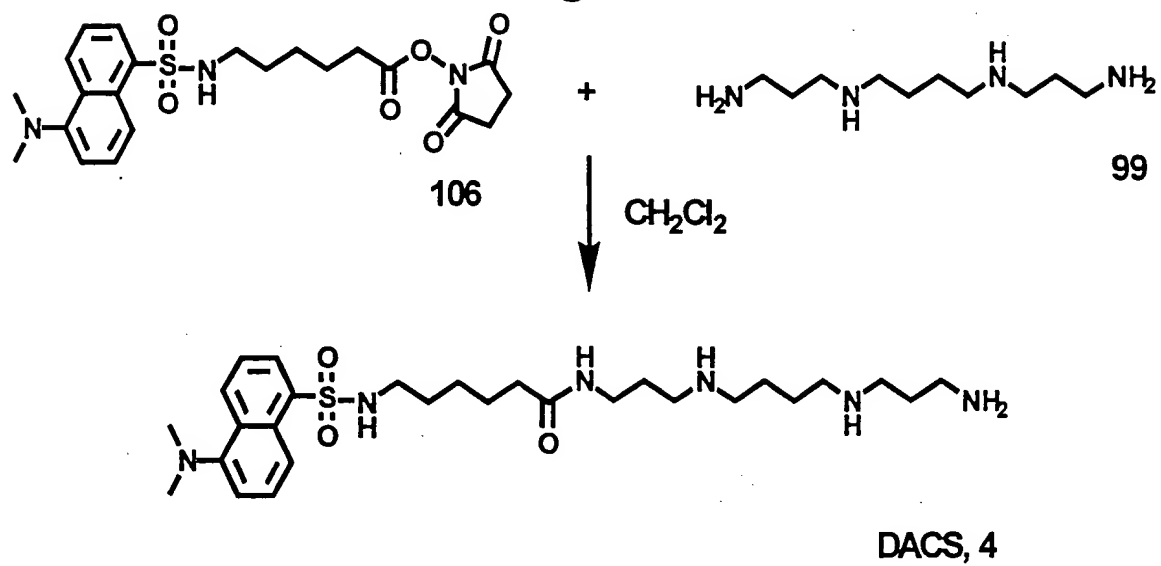


Fig. 9

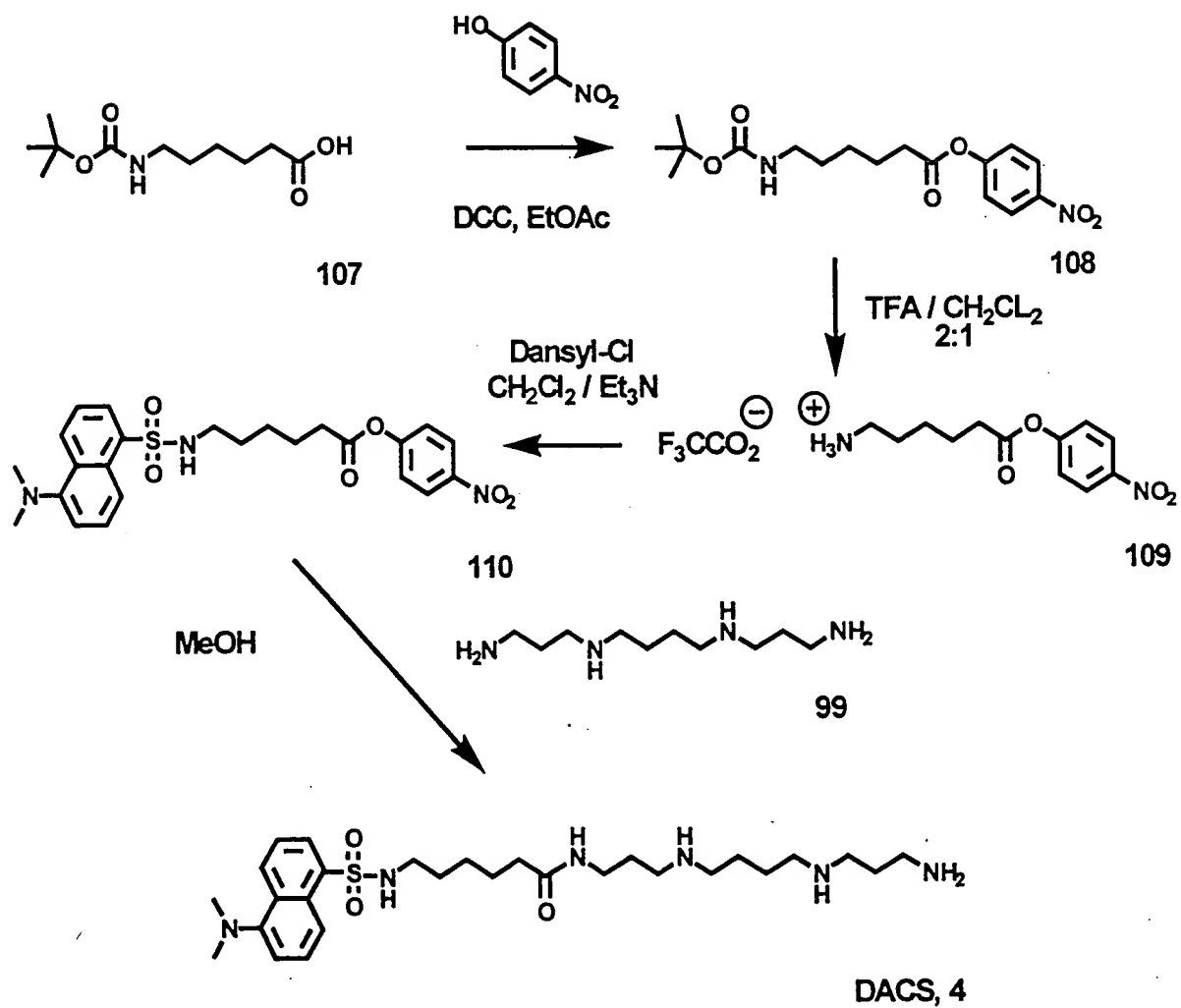
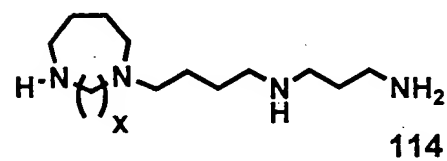
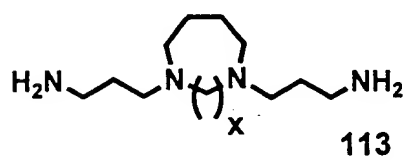
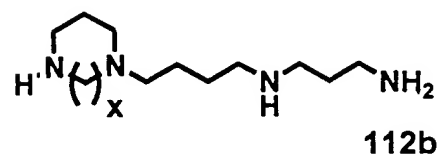
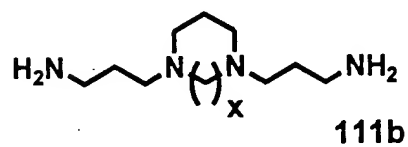
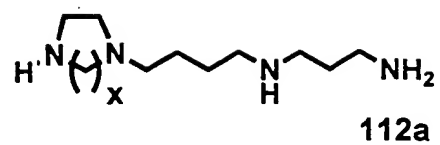
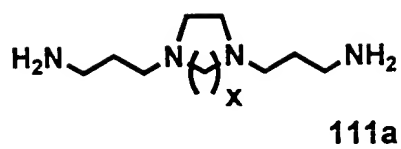




Fig. 10



$x = 1 \text{ to } 4$

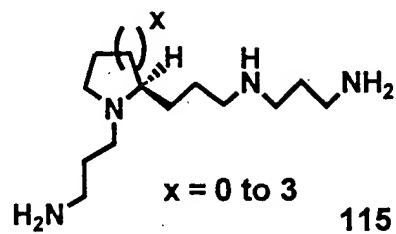


Fig. 11

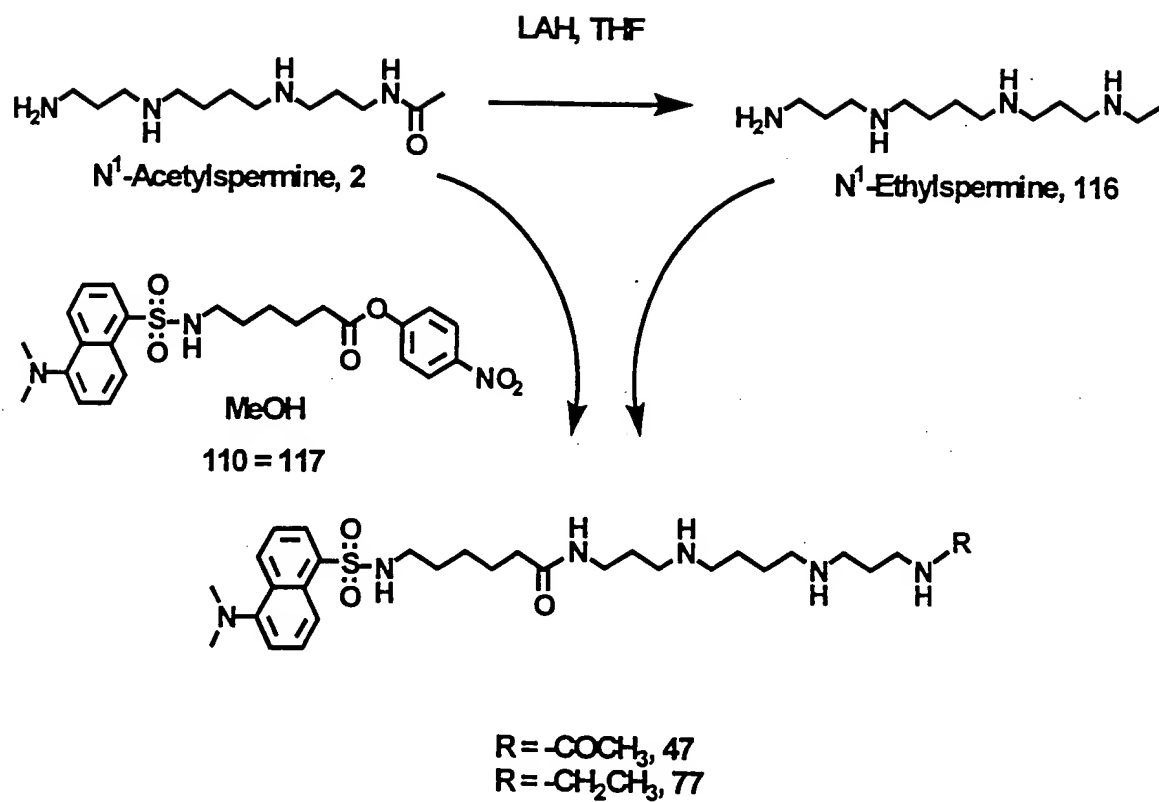
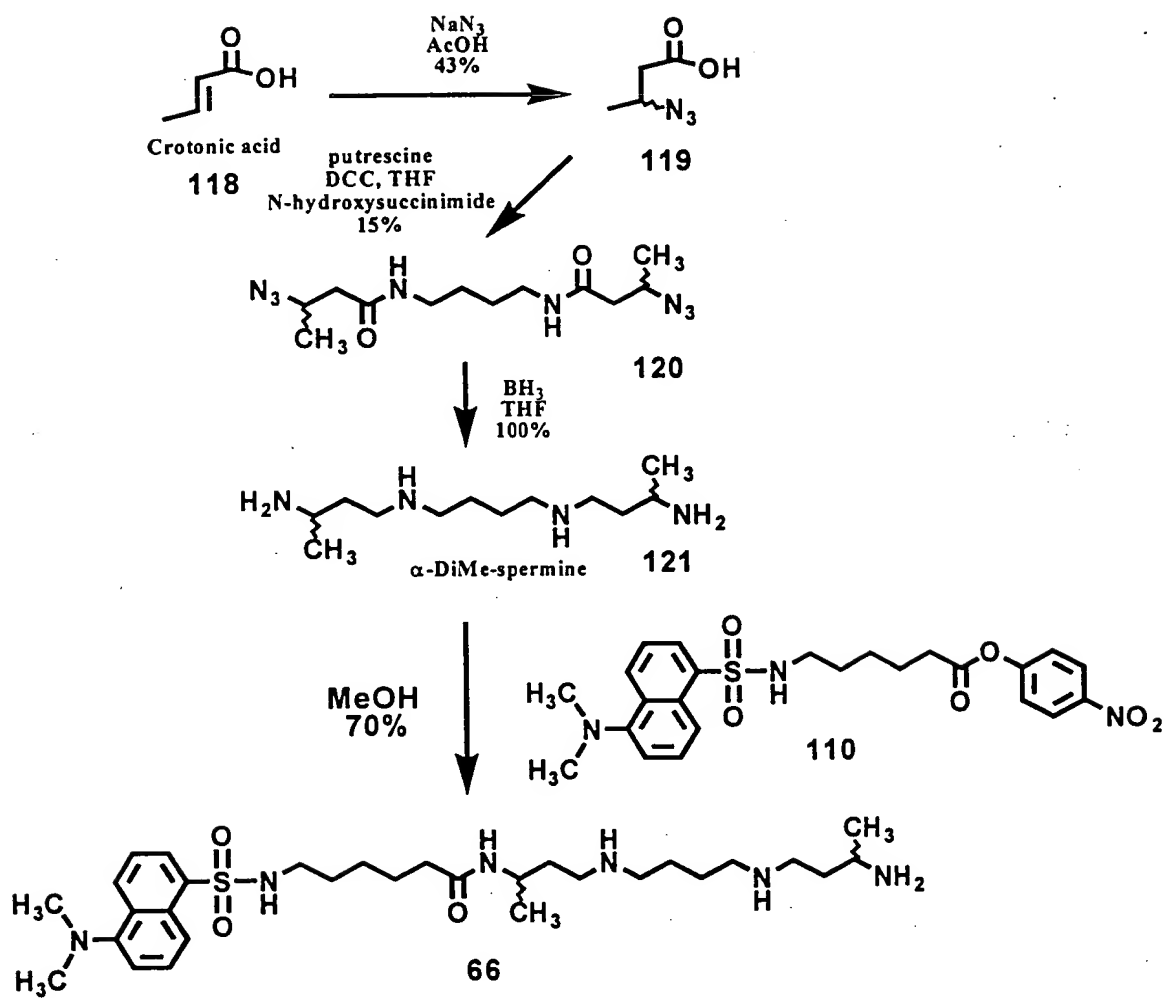
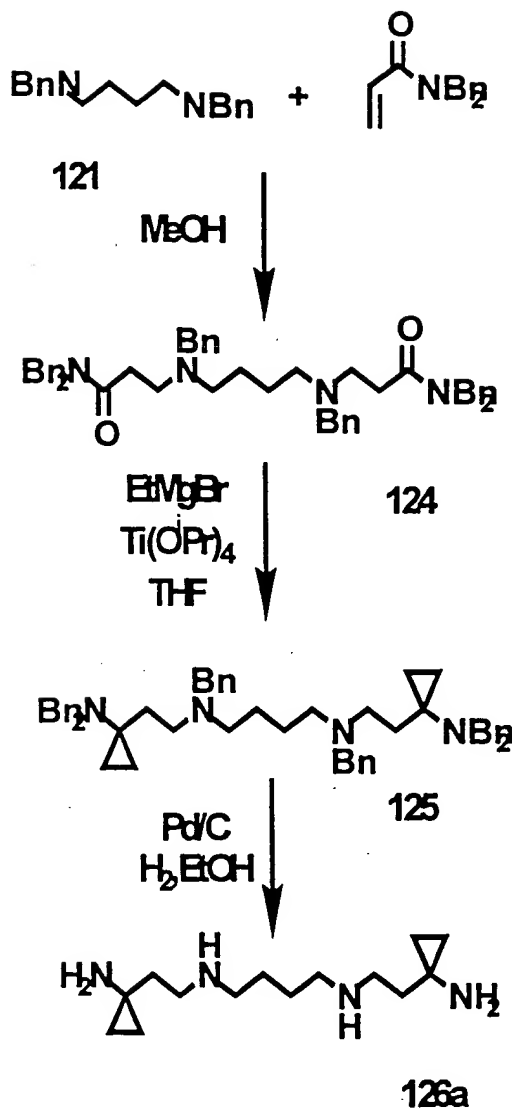


Fig. 12



004713612-11400

Fig. 13



Other analogs:

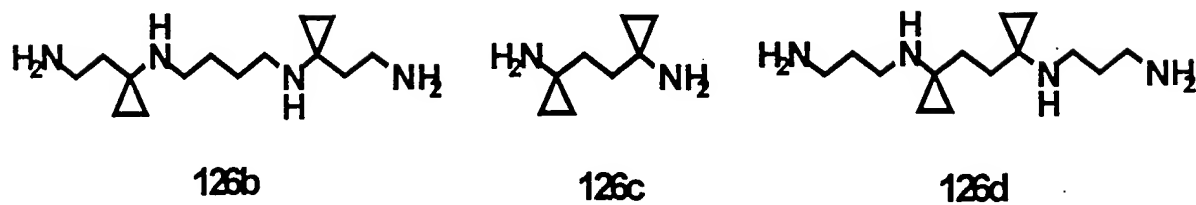
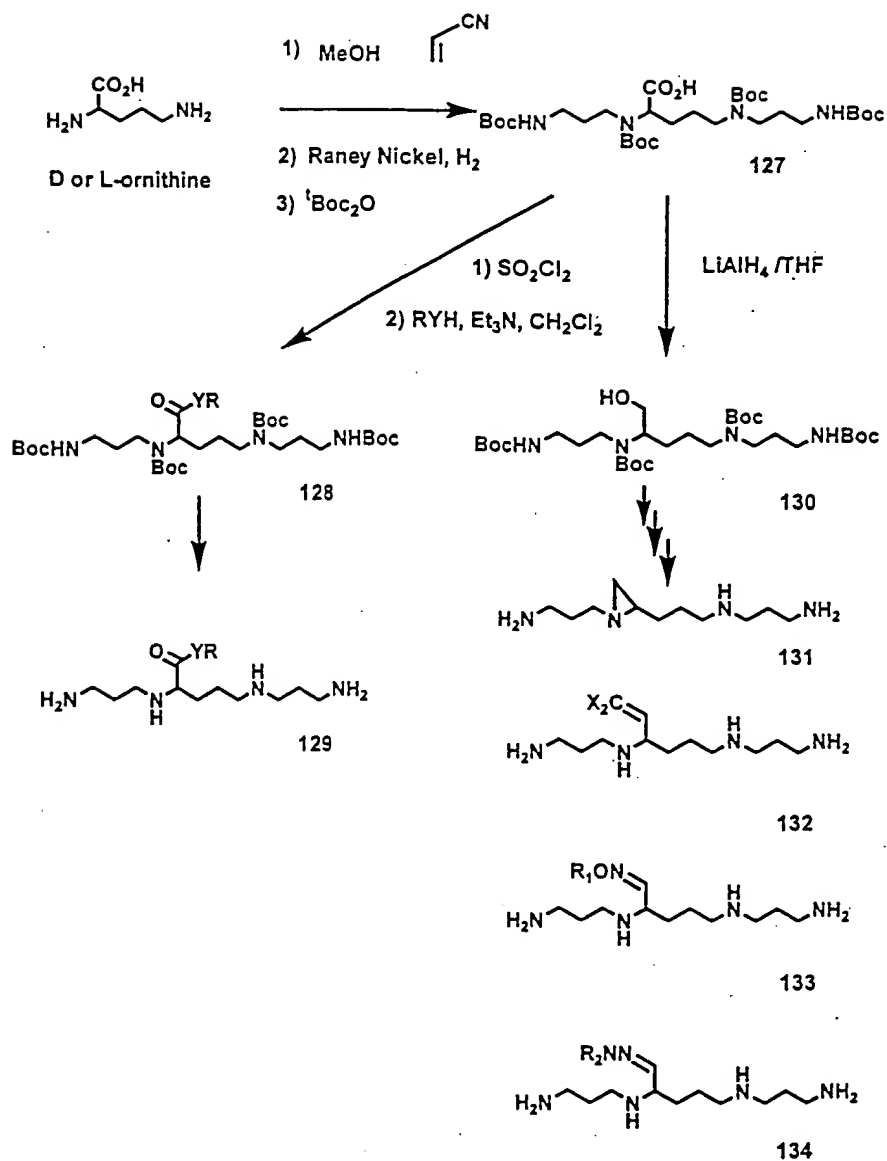
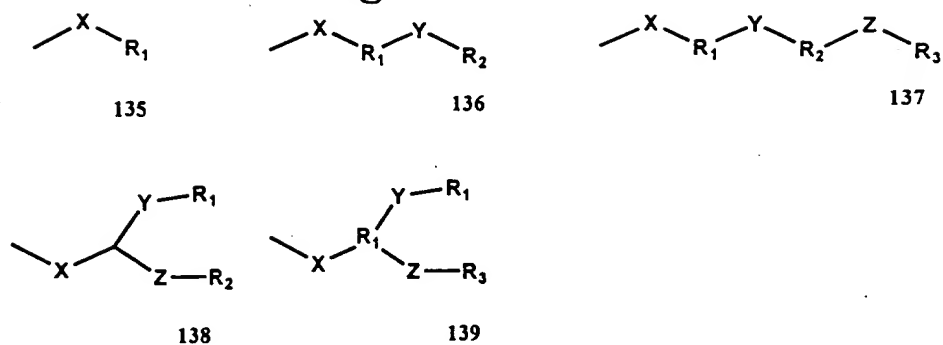


Fig. 14



**Fig. 15**

Where  $\text{X}=\text{spacer}_1$ ;  $\text{Y}=\text{spacer}_2$ ; and  $\text{Z}=\text{spacer}_3$ ; and

$\text{R}_1$ ,  $\text{R}_2$ , and  $\text{R}_3$  can be alicyclic, aromatic, or heterocyclic

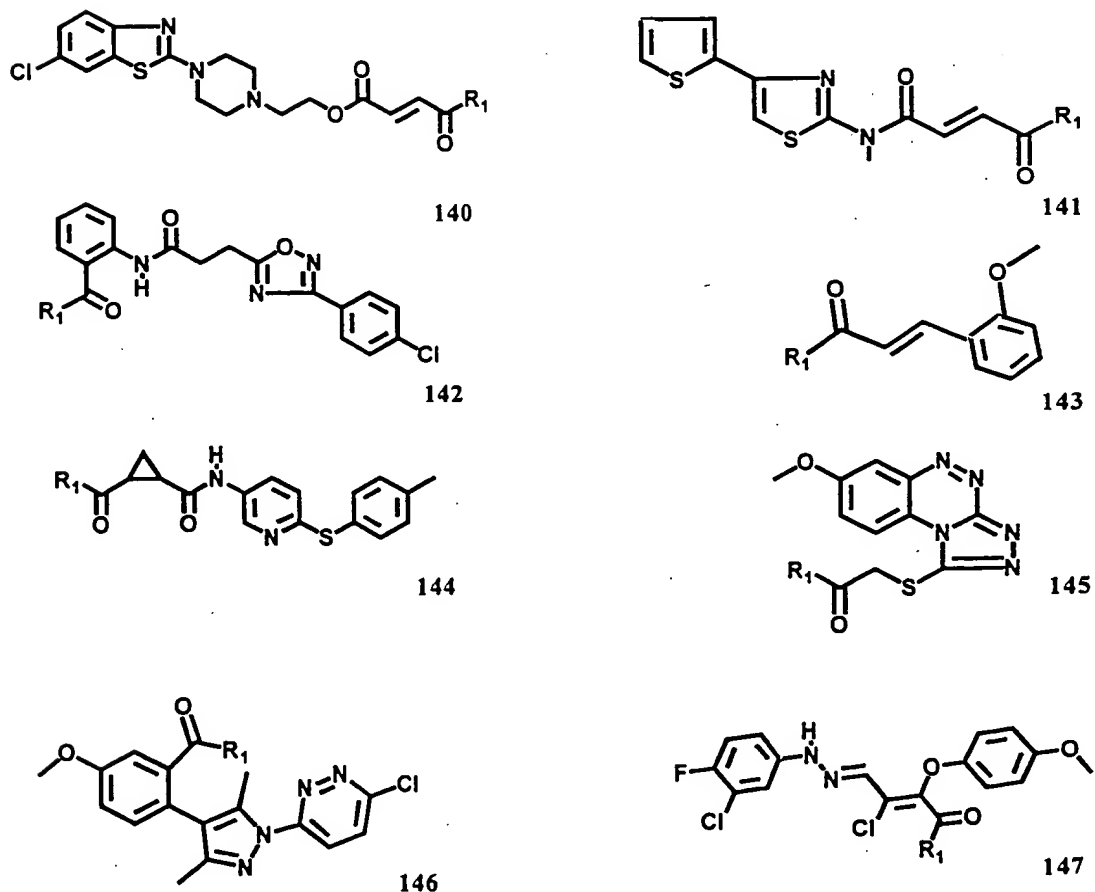
**Fig. 16**

Fig. 17

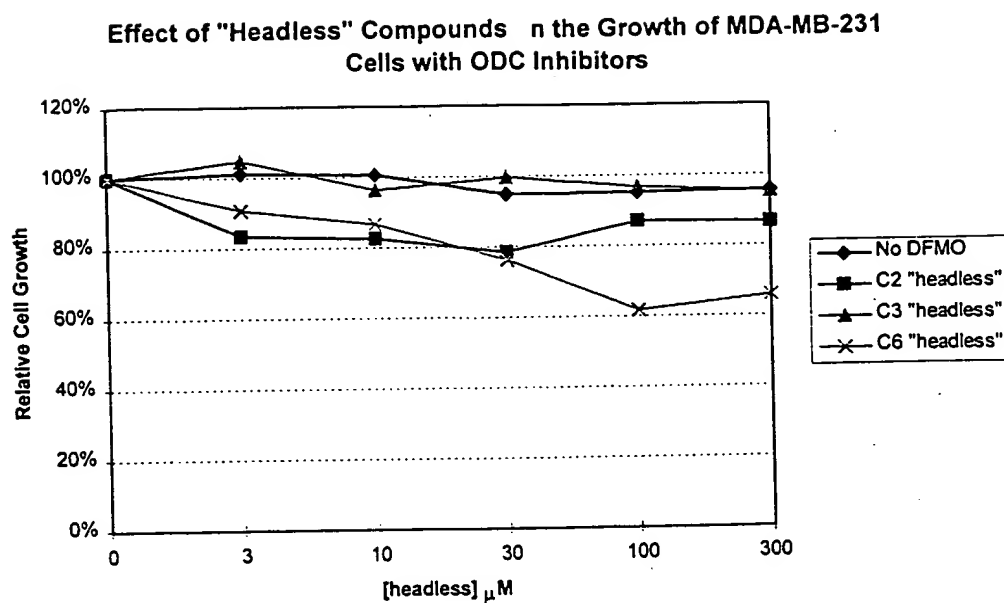


Fig. 18

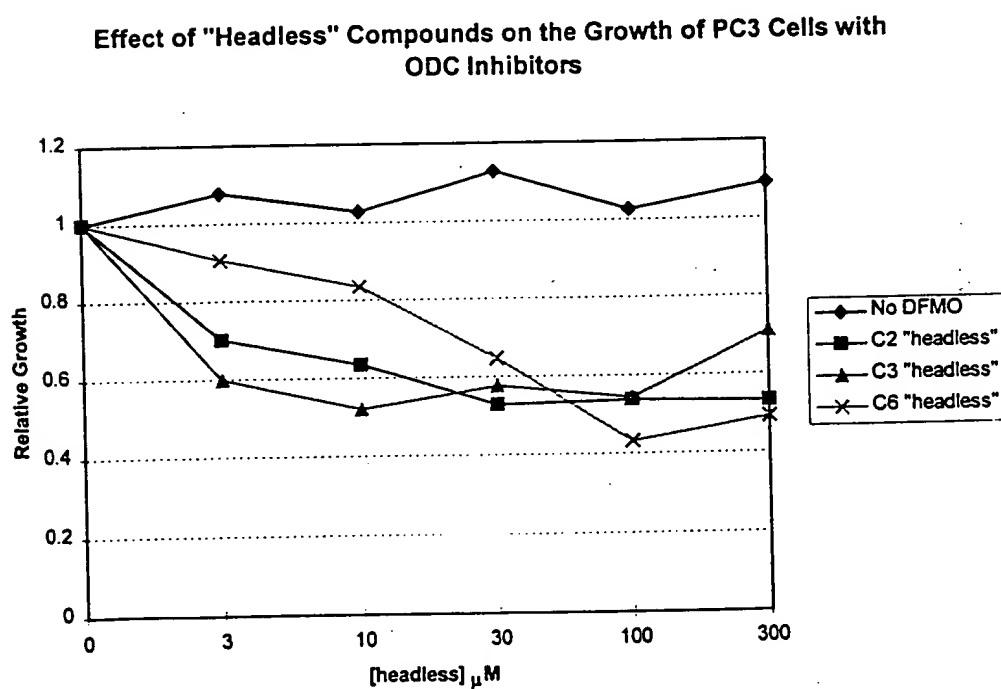
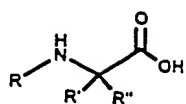


Fig. 19



153

stereochemistry:  
L is S, D is R

<u>R'</u>		<u>R'</u>		<u>R'</u>	
-H	Gly	HS-	Cys	HO-	Ser
-CH <sub>3</sub>	Ala	-S-CH <sub>3</sub>	Met	OH-	Thr
	Val		Asn		His
	Leu		Gln		Pro
	Ile		Asp		Lys
	Phe		Glu		Arg
	Tyr		Trp		

Where R=head group; R''= H, -CH<sub>3</sub>-, -CH<sub>2</sub>CH<sub>3</sub>-, -CHF<sub>2</sub>

09713513-11400



Fig. 20

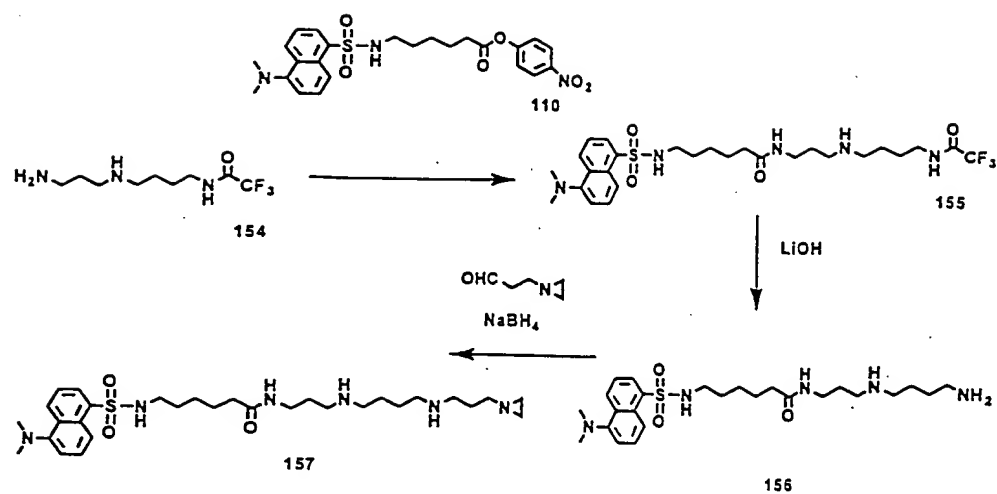
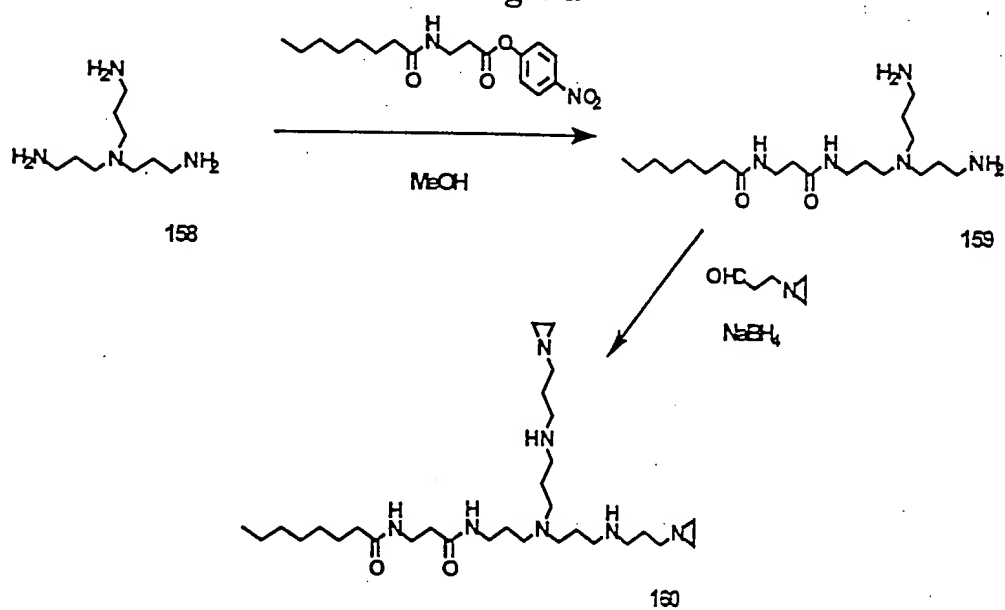
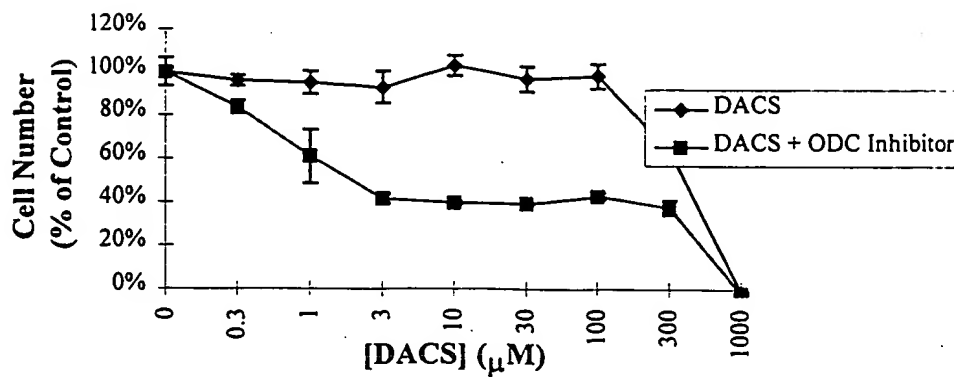


Fig. 21



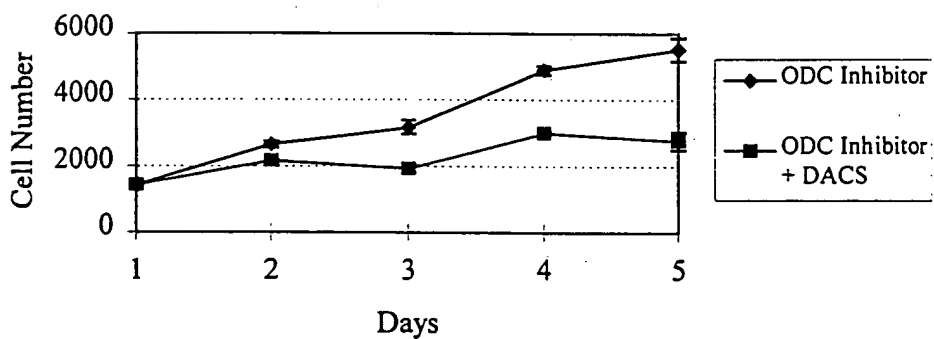
**Fig. 22**

**DACS with an ODC Inhibitor Enhances the Growth-Inhibition of MDA-MB-231 Breast Carcinoma Cells**

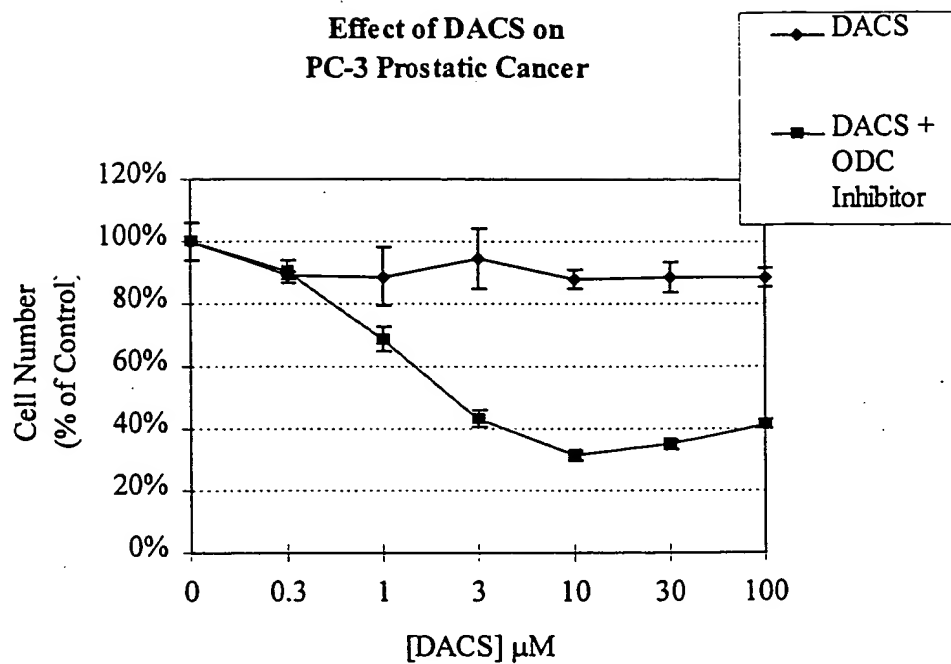


**Fig.23**

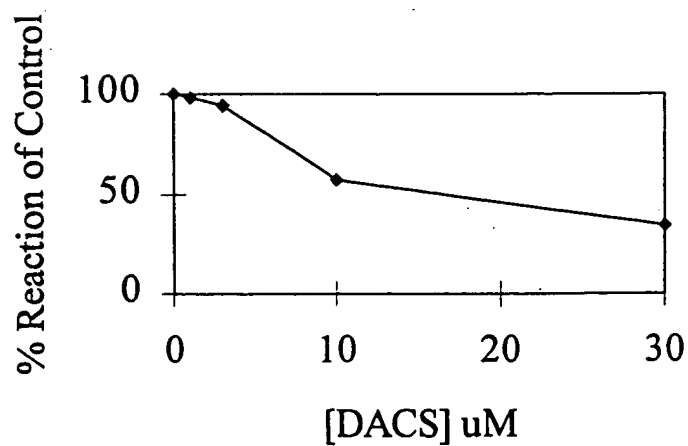
**DACS Inhibits Growth in the Presence of 1.0  $\mu\text{M}$  Spermidine**

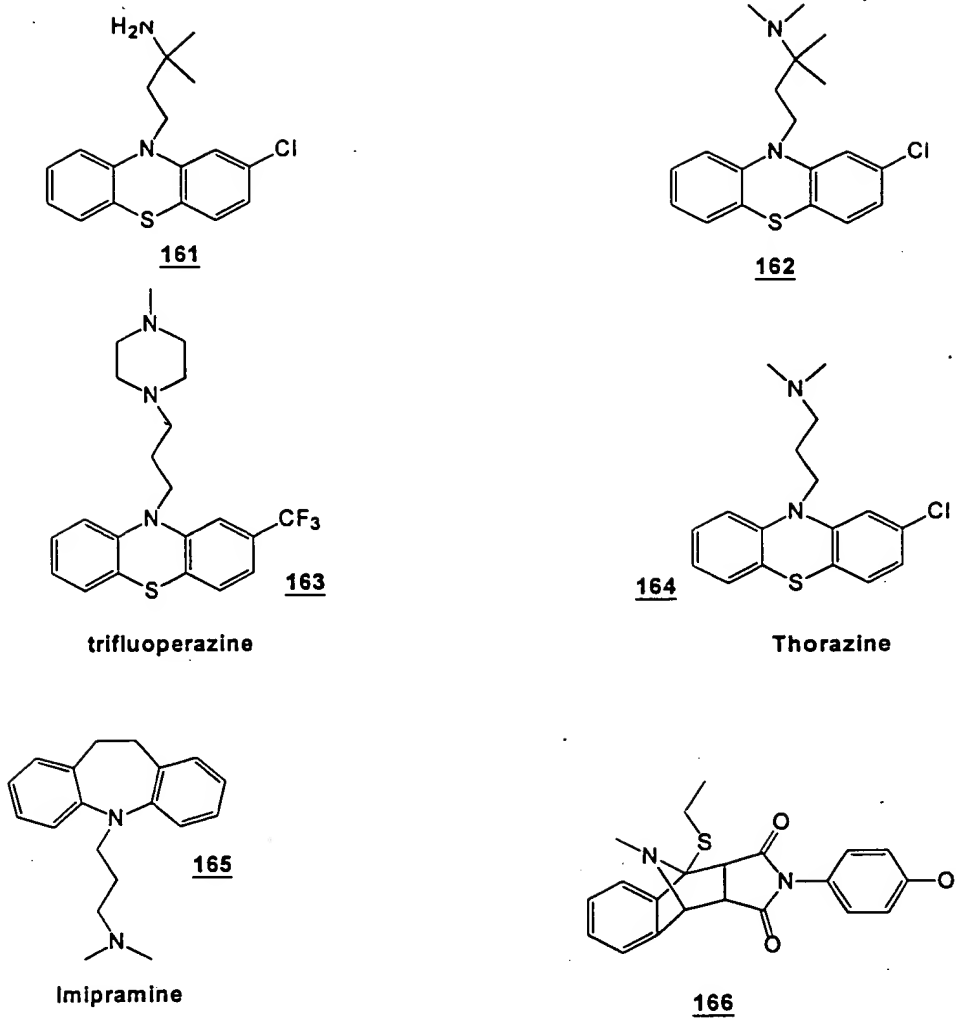


**Fig. 24**



**Fig. 26**





**Fig. 25**

Fig. 27

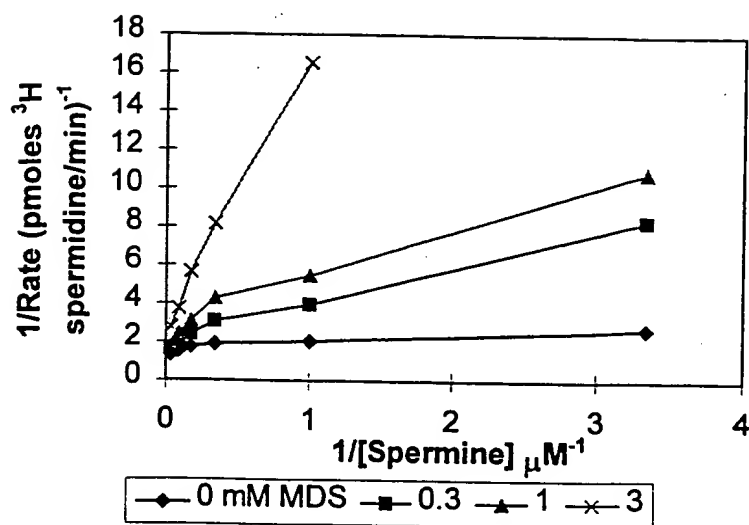


Fig. 28

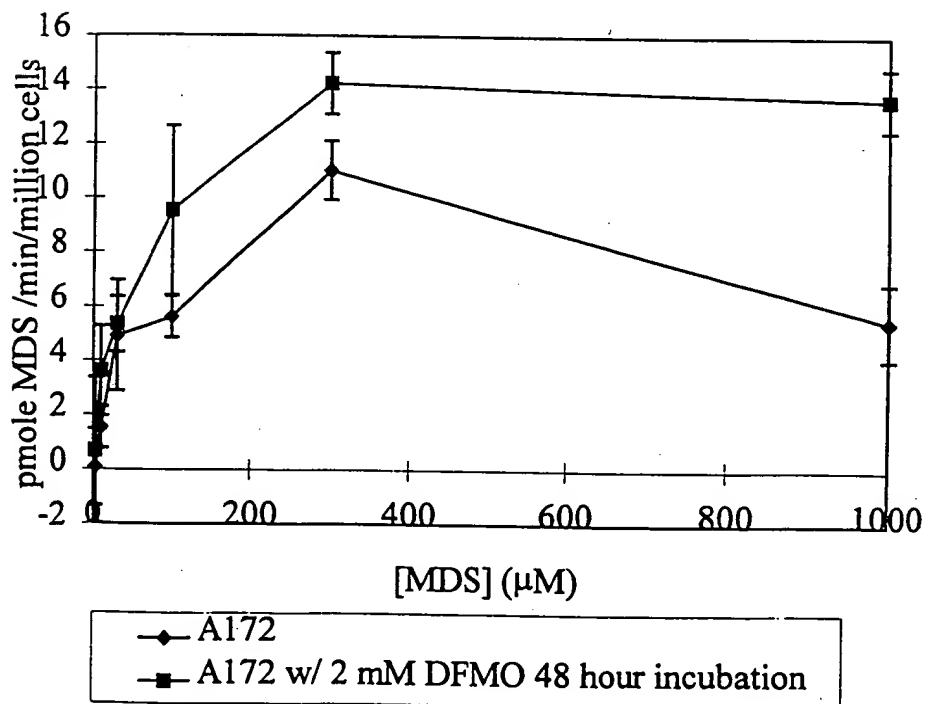


Fig. 29

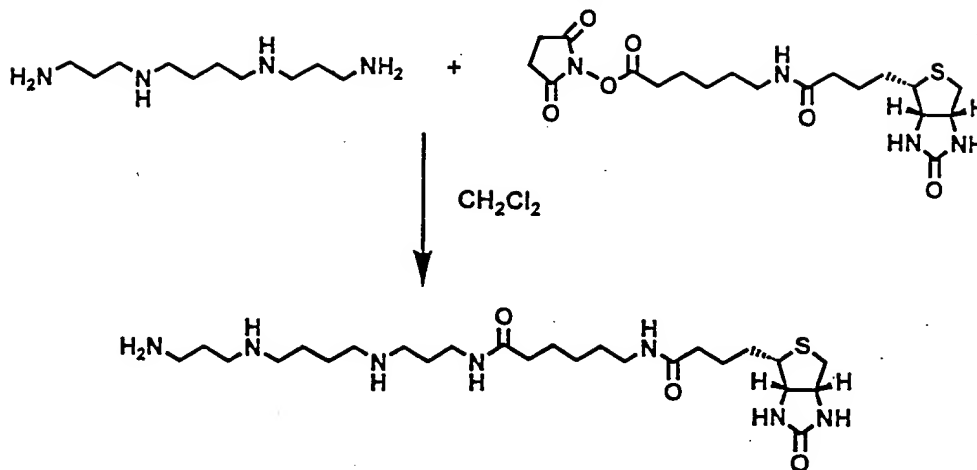


Fig. 30

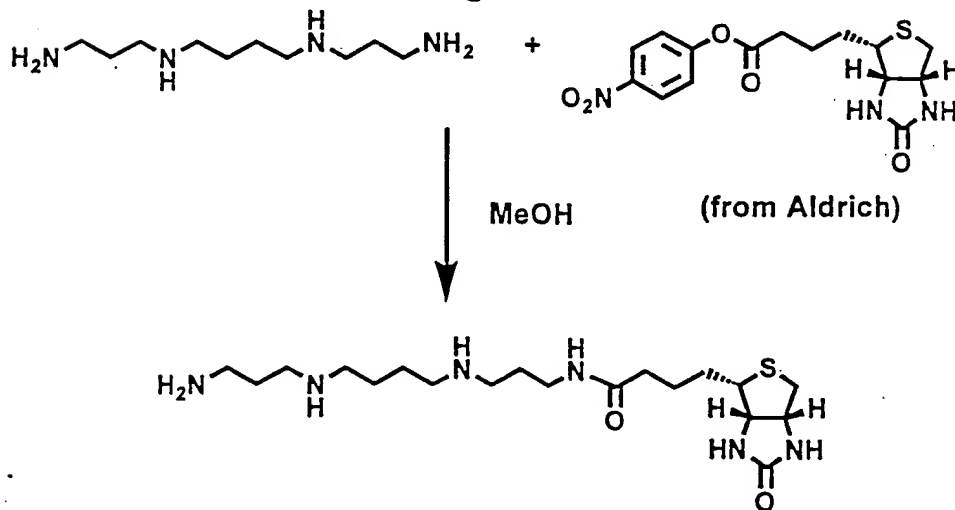
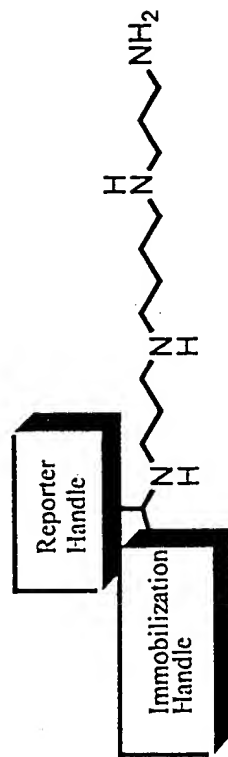
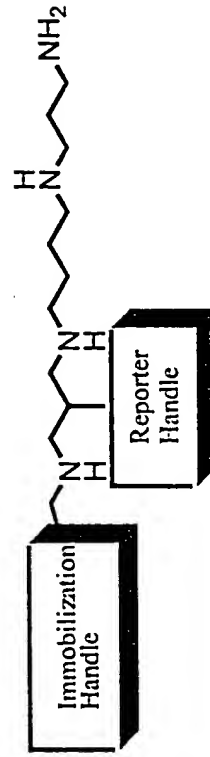


Fig. 31

A. Reporter and Immobilization handles are both N<sup>1</sup>-terminal



B. Reporter Handle is internal and Immobilization handle is N-terminal.



C. Immobilization and Reporter handles are both N<sup>1</sup> and N<sup>12</sup> terminal, respectively

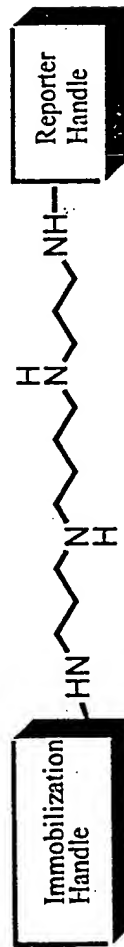
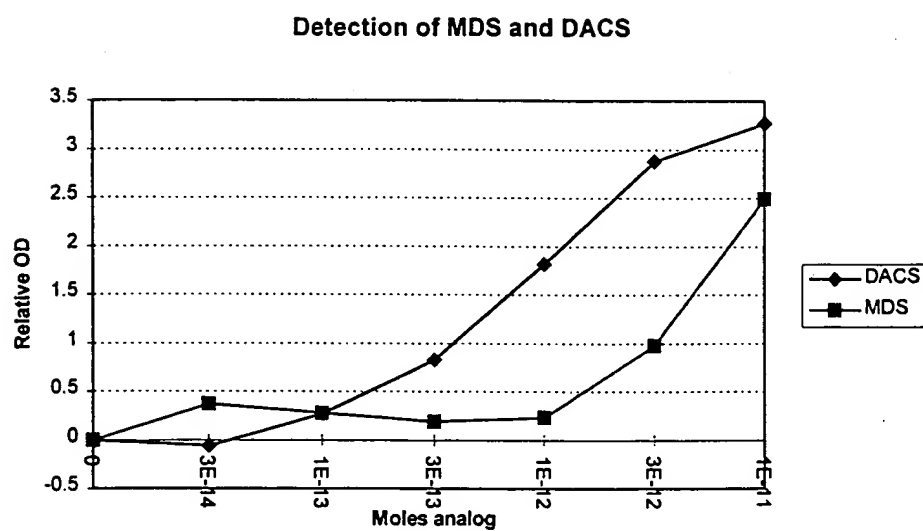


Fig. 32



09713512 111400



Fig. 33

# General Scheme

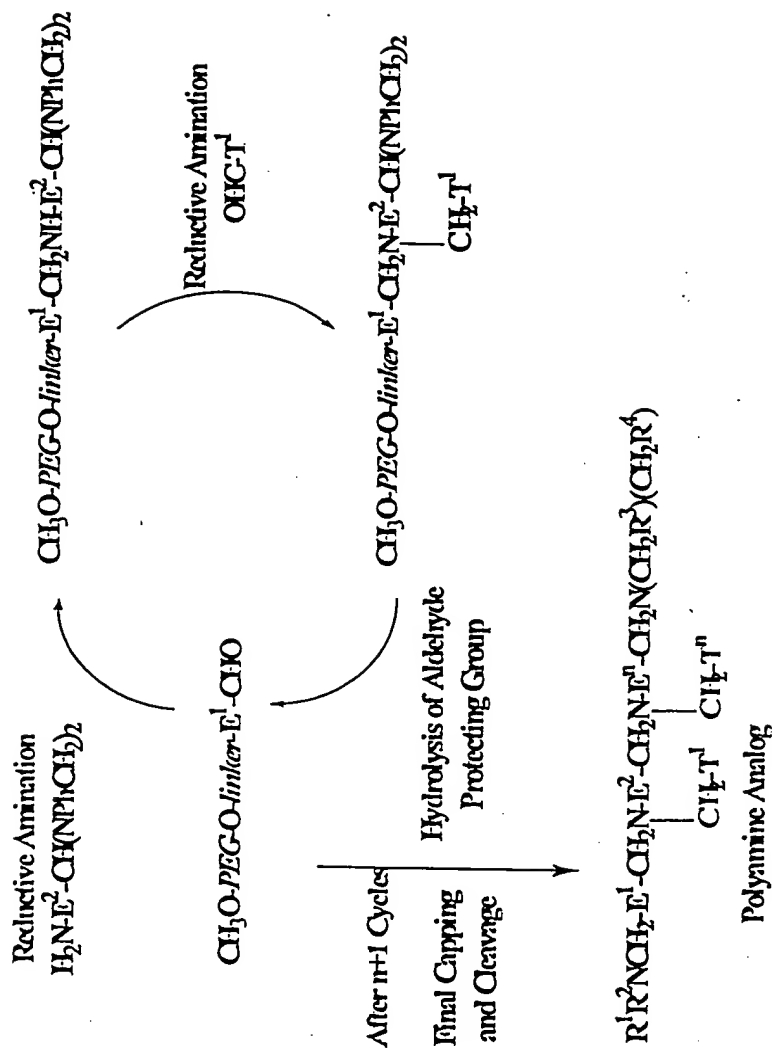


Fig. 34

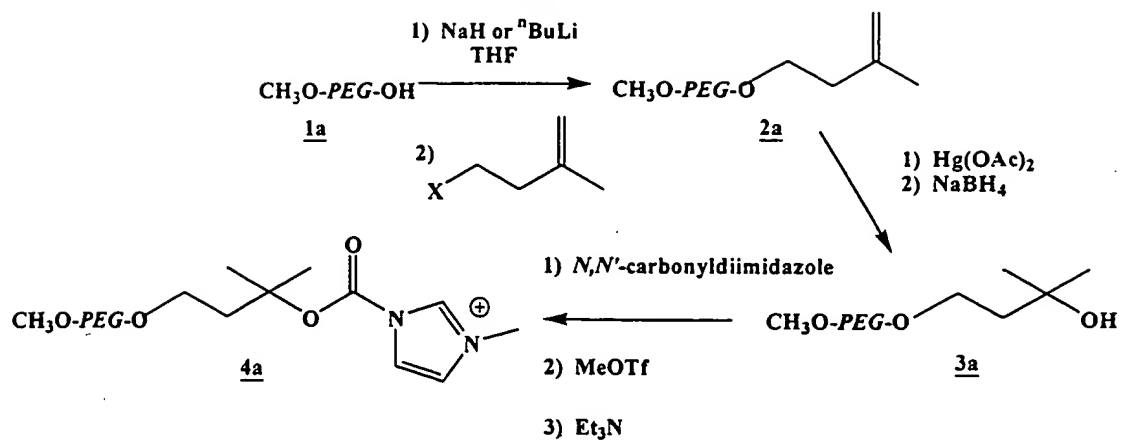


Fig. 35

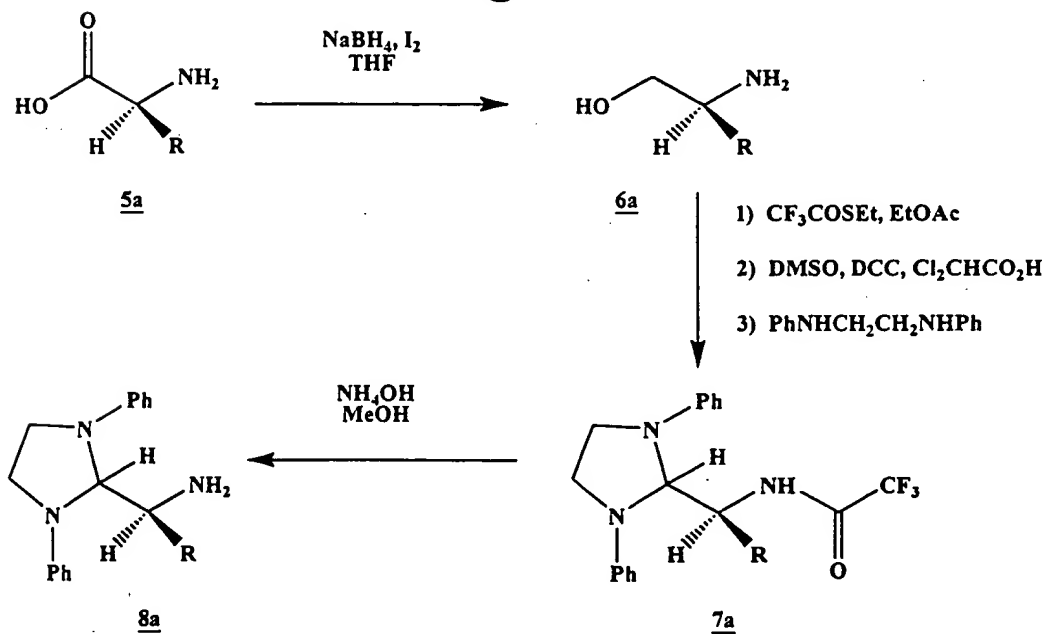


Fig. 36

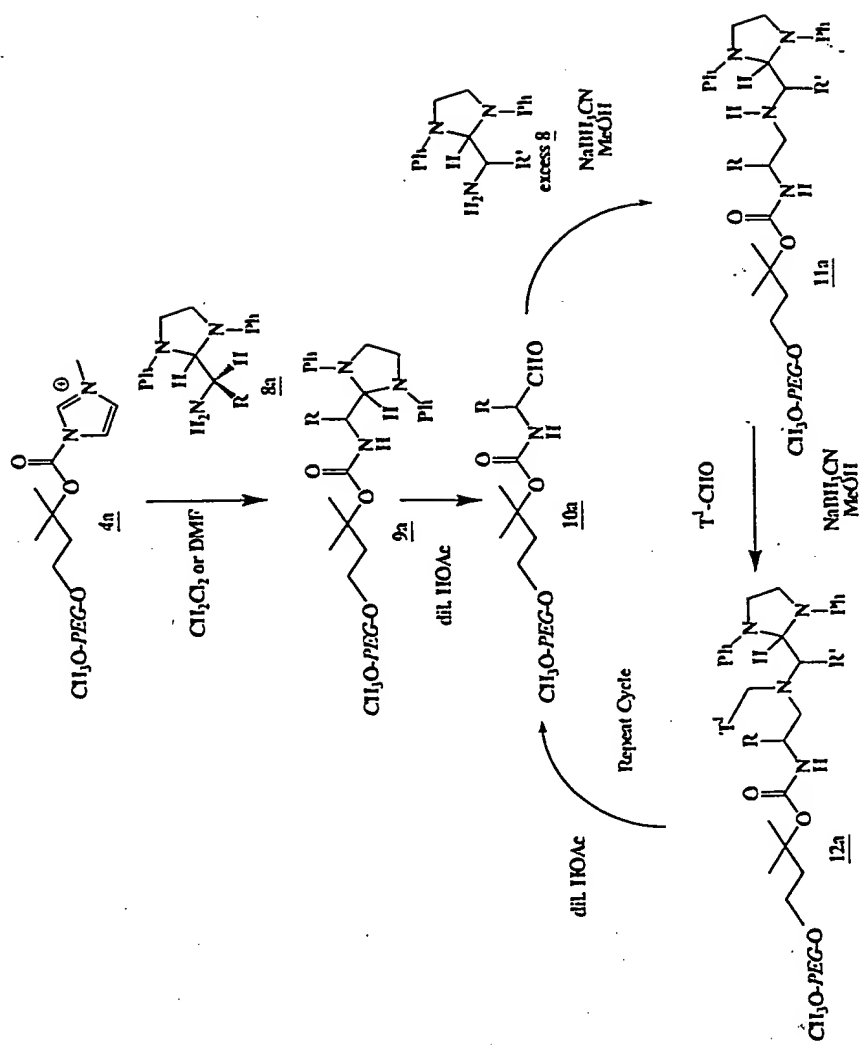
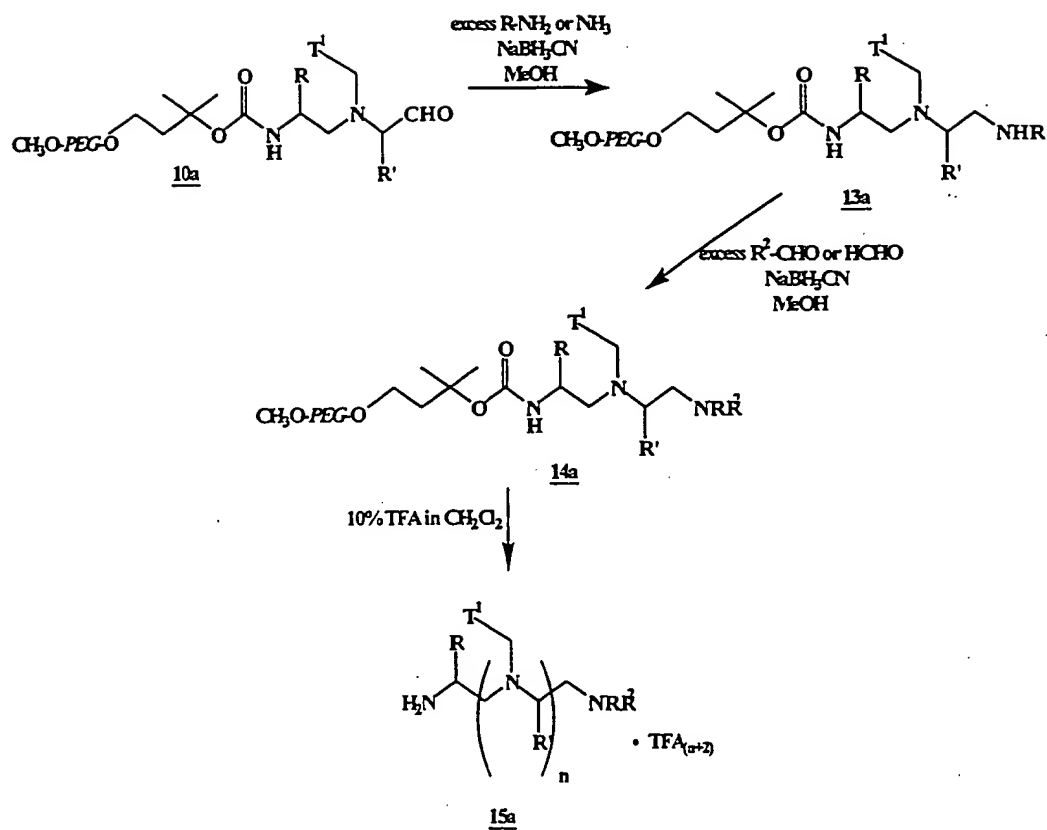
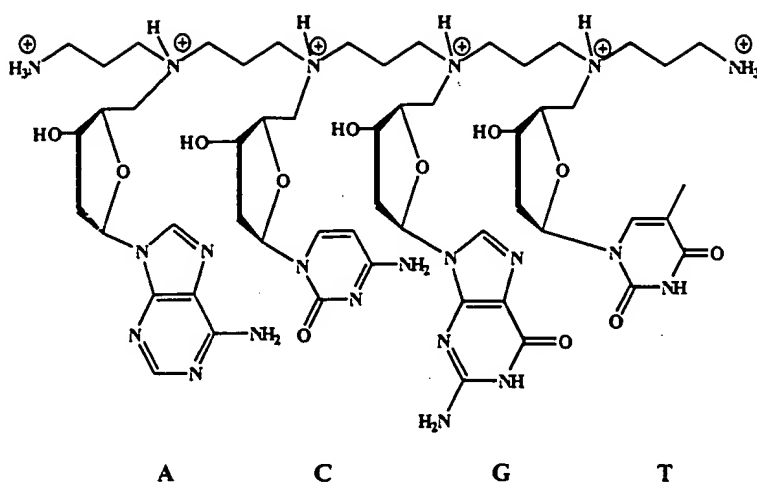


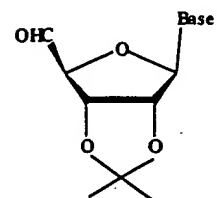
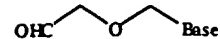
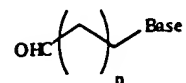
Fig. 37



**Fig. 38**



### Other Base / Polyamine Linkers As Terminators



**Fig. 39**

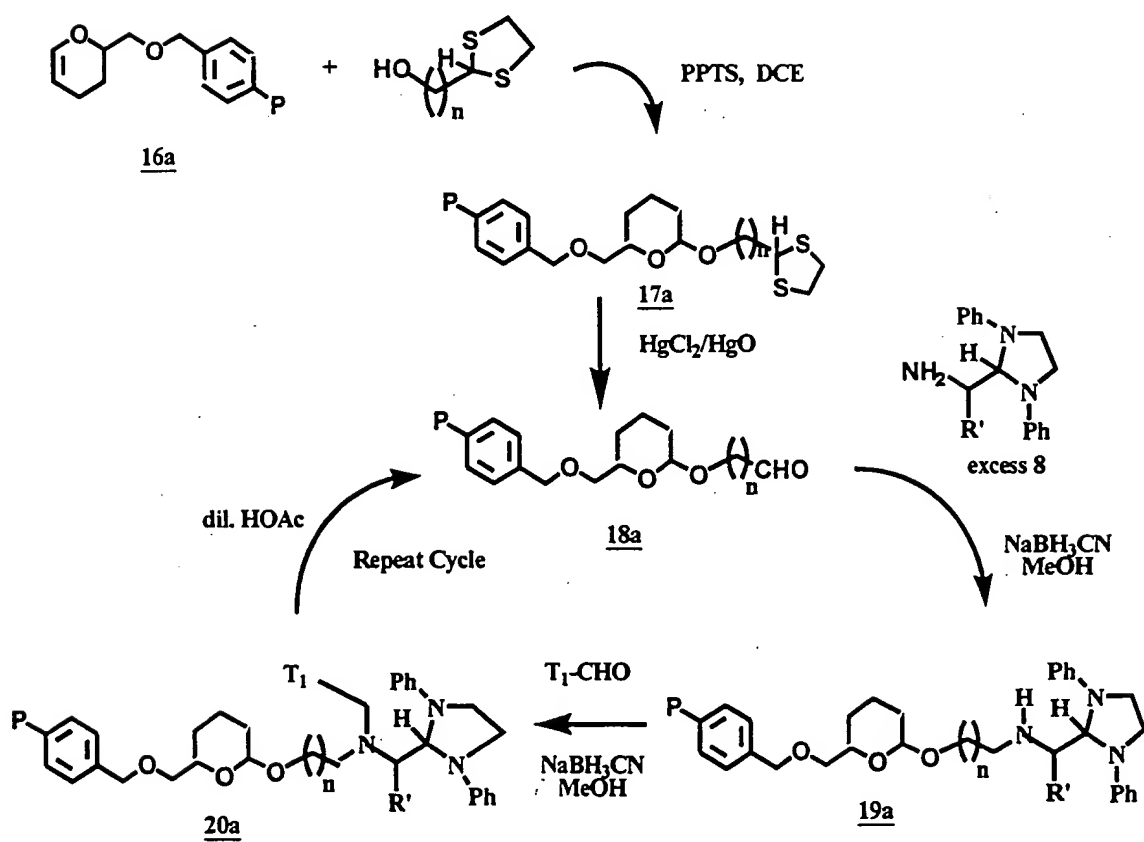


Fig. 40

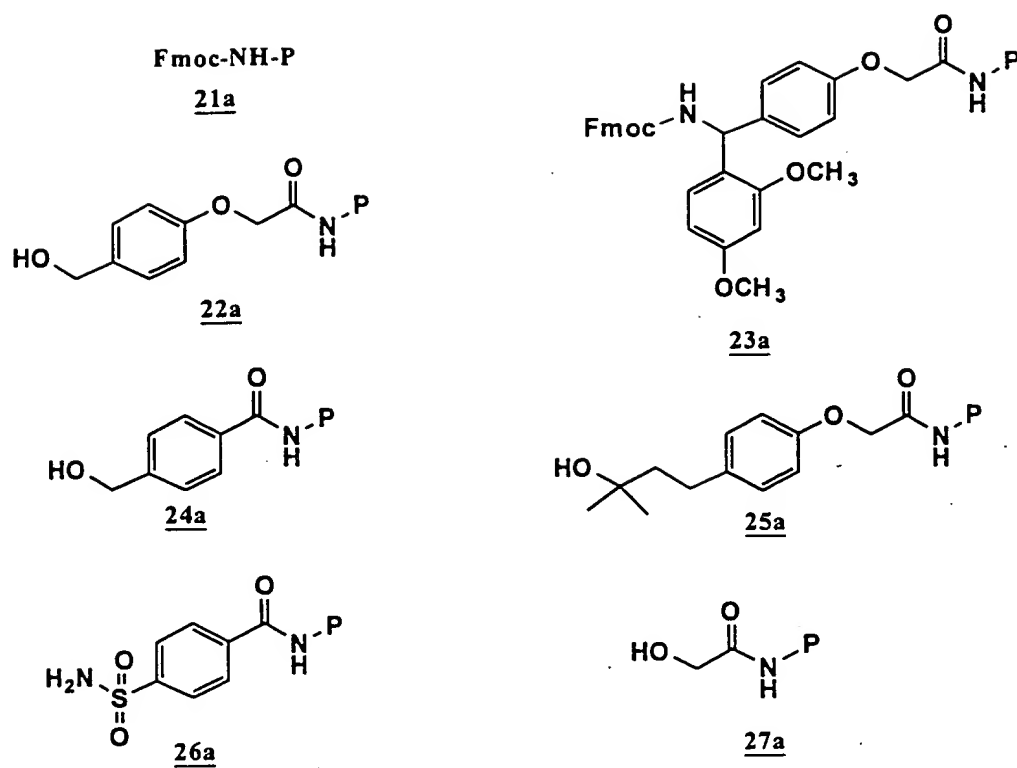


Fig. 41

